AN 2001:639971 CAPLUS
TI GPCR agonist design using privileged structures
AU Patchett, A.
CS Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, 07065, USA
SO Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001 (2001), MEDI-152 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69BUZP
DT Conference; Meeting Abstract
LA English
AB The derivatization of GPCR privileged structures with capped amino acids and dipeptides has afforded potent and selective small mol. agonists of much larger peptide ligands. The approach has been successful in the synthesis of **growth hormone** secretagogues, somatostatin mimetics and more recently **melanocortin** MC-4 agonists. Modeling and mutagenesis studies have been undertaken to help rationalize the agonist activities of several of these relatively small peptidomimetics.

AN 2002:850626 CAPLUS
DN 138:70708
TI Weight loss at high altitude
AU Tschop, Matthias; Morrison, Katherine M.
CS Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN, USA
SO Advances in Experimental Medicine and Biology (2001), 502(Hypoxia), 237-247
CODEN: AEMBAP; ISSN: 0065-2598
PB Kluwer Academic/Plenum Publishers
DT Journal; General Review
LA English
AB A review. Loss of appetite and wt. are frequently obsd. at altitudes above 5000m. However, the pathophysiol. behind changes in body compn. at extreme altitude is still not fully understood. Proper acclimatization to altitude and high caloric intake minimizes, but can not completely prevent significant wt. loss under the influence of hypobaric hypoxia. The discovery of leptin in 1994 has initiated a new research area investigating mol. networks that connect peripheral organs with the central nervous system to sense and regulate energy intake as well as energy expenditure. Since then, a whole microcosm of new hormones, neurotransmitters and receptors has been discovered and studied with respect to body wt. control. Those agents include neuropeptide Y (NPY), agouti-related protein (AGRP), **melanocortin**, receptors (MC-R), cocaine-amphetamine regulated transcript (CART), proopiomelanocortin (POMC), orexin A and B (hypocretins), melanin-concg. hormone (MCH) and ghrelin (endogenous ligand of the **growth hormone** secretagogue receptor). This overview will introduce the current concepts of the mol. control of energy homeostasis and attempt to reexamine the effects of altitude on appetite and body compn. in light of these concepts. An overview of studies on changes of appetite and body compn. at high altitude will be followed by the presentation of recent data on changes of endocrine parameters at hypobaric hypoxia that could be involved in the pathophysiol. of wt. loss.
RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 2002:204581 CAPLUS
DN 136:319491
TI The arcuate nucleus as a conduit for diverse signals relevant to energy homeostasis
AU Cone, R. D.; Cowley, M. A.; Butler, A. A.; Fan, W.; Marks, D. L.; Low, M. J.
CS Vollum Institute, Oregon Health and Science University, Portland, OR, 97201-3098, USA
SO International Journal of Obesity (2001), 25(Suppl. 5), S63-S67
CODEN: IJOBDP; ISSN: 0307-0565
PB Nature Publishing Group
DT Journal; General Review
LA English
AB A review. Arcuate nucleus neurons are known to be responsive to a wide array of hormones and nutrients, including leptin, insulin, gonadal steroids and glucose. In addn. to potential transport mechanisms, peripheral substances may access these neurons via arcuate cell bodies in and projections to the median eminence, a region considered to be a circumventricular organ. The arcuate is a potent site of leptin action, probably mediating a component of leptin's effects via arcuate neuropeptide Y/agouti-related peptide (NPY/AgRP) and pro-opiomelanocortin (POMC) neurons, and implicating this structure in the long-term control of energy stores. However, ghrelin, the endogenous ligand of the **growth hormone** secretagogue receptor, may also stimulate feeding and wt. gain, in part through action on receptors in arcuate NPY neurons. Since ghrelin is secreted by the stomach upon content depletion, with a half-life of no more than an hour, the arcuate nucleus may also be important in sensing and responding to acute changes in nutrients. The authors have developed a system for recording from arcuate POMC neurons using a mouse contg. a transgene in which the POMC promoter is driving expression of the green fluorescent protein (GFP). In these mice, 99% of the .beta.-endorphin pos. neurons express GFP, making whole cell patch clamp recordings from the sparsely distributed POMC neurons facile. All of the POMC neurons appear to be activated by leptin, via two different mechanisms, while approx. 30-50% of the neurons appear to be inhibited by a gamma-MSH specific agonist. The latter result suggests that the **melanocortin**-3 receptor (MC3-R) may act as an autoinhibitory receptor on some POMC neurons. This hypothalamic slice prepn. also confirms the responsiveness of arcuate POMC neurons to a wide variety of nutrients and hormones. Thus the arcuate **melanocortin** system is best described as a conduit of many diverse signals involved in energy homeostasis, with leptin acting tonically to regulate the responsiveness of the circuit to a wide variety of hormones and nutrients.
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 2001:880485 CAPLUS
DN 136:131833
TI Identification of a novel GH isoform: a possible link between GH and melanocortin systems in the developing chicken eye
AU Takeuchi, Sakae; Haneda, Masahiko; Teshigawara, Kiyoshi; Takahashi, Sumio
CS Department of Biology, Faculty of Science, Okayama University, Okayama, 700-8530, Japan
SO Endocrinology (2001), 142(12), 5158-5166
CODEN: ENDOAO; ISSN: 0013-7227
PB Endocrine Society
DT Journal
LA English
AB The present study was conducted to assess the possibility that **growth hormone** (GH) may play a role in ocular development by detg. whether GH is expressed in the eye of the chicken during development. In the 17-day (d)-old embryo, immunocytochem. detected immunoreactive GH in retinal pigment epithelial (RPE) cells. Characterization of GH mRNA expressed in the eye by RT-PCR and rapid amplification of cDNA 5'-ends revealed it to be a novel GH mRNA transcribed from the middle of the intron 3 of the chicken GH (cGH) gene. The deduced protein, designated small GH isoform (s-cGH), was a cytosolic protein of 16.5 kDa with 140 amino acid (aa) residues, lacking the signal peptide and the N-terminal 71 aa residues of 22-kDa cGH, replacing them with 20 aberrant aa residues, and identical to 22-kDa cGH for the C-terminal 120-aa residue portion. Western blotting detd. the mol. size of immunoreactive GH in RPE cells to be 80-84 kDa, similar to the computed mol. mass of s-cGH/GH receptor complex. Furthermore, RT-PCR demonstrated that GH receptor mRNA, but not s-cGH mRNA, was expressed in RPE cells. These results suggest that RPE cell is 1 of the target cells of s-cGH in the eye. During embryonic development, the immunoreactivity for s-cGH in RPE cells was initially obsd. on embryonic d 10, and the staining intensity increased and peaked on embryonic d 17. By hatching, s-cGH immunoreactivity in RPE cells was gradually decreased, and it was not detectable after hatching. This ontogenetic staining pattern correlates well with the pattern of the prodn. of .alpha.MSH in RPE cells. The cell type expressing s-cGH remains to be identified; however, our findings imply a possible involvement of GH in the regulation of ocular development by acting on the intraocular **melanocortin** system in the chicken.
RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

DN 128:110853
TI Melanocortin-4 receptor in screening for compounds useful in the regulation of body weight
IN Lee, Frank; Huszar, Dennis; Gu, Wei
PA Millennium Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9747316	A1	19971218	WO 1997-US9969	19970609
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5908609	A	19990601	US 1996-662560	19960610
	US 5932779	A	19990803	US 1997-780749	19970108
	AU 9733836	A1	19980107	AU 1997-33836	19970609
	AU 723135	B2	20000817		
	EP 915706	A1	19990519	EP 1997-929878	19970609
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9709684	A	20000509	BR 1997-9684	19970609
	JP 2002514041	T2	20020514	JP 1998-501745	19970609
PRAI	US 1996-662560	A	19960610		
	US 1997-780749	A	19970108		
	US 1997-870511	A	19970606		
	WO 1997-US9969	W	19970609		

AB The present invention relates to drug-screening assays, and diagnostic and therapeutic methods for the treatment of body wt. disorders, such as obesity, anorexia and cachexia, utilizing the melanocortin 4 receptor (MC4-R) as the target for intervention. The invention also relates to compds. that modulate the activity or expression of the MC4-R, and the use of such compds. in the treatment of body wt. disorders.

IT 9001-78-9, Alkaline phosphatase 9002-72-6, **Growth hormone** 9030-08-4, Glucuronosyltransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene encoding; **melanocortin**-4 receptor in screening for compds. useful in the regulation of body wt.)